Ciguatera: A review

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Hawaii State Department of Health epidemiological records were reviewed for cases of ciguatera poisoning for the entire state, from January 1984 through December 1988. During the 5 year interval, the numbers of ciguatera poisoning incidents, number of cases, and date of onset were recorded, as well as age and sex of individuals involved. The place of catch of each fish was noted as well as whether or not the fish was obtained commercially. The parts of the fish consumed were also recorded.

A total of 150 ciguatera incidents occurred during this period, involving 462 individuals for an average annual incidence rate of 8.7/100,000 population. The 3 most frequently implicated species of fish were the Carangoides species (jack or papio or ulua), Ctenochaetus strigosus (surgeon fish or kole), and Aphareus furcatus (fork-tailed snapper or waha nui); however, more than 50 species of fish had caused one or more outbreaks. The most frequently implicated areas of the toxic fish were the Kona coast as well as the South Point of the island of Hawaii, and the Napali coast of the island of Kauai. Of the 150 outbreaks, 32 (21%) were related to commercial fish. The rest were related to sportfishing.

Introduction and history

Ciguatera fish poisoning is a disease which results from the ingestion of reef fish. For many years it was primarily a concern of those residing in the tropics or subtropics. However, it is becoming increasingly significant for fish-eaters in temperate areas of the world as well, as fish has become more popular and quick air delivery of fresh fish is a reality[1-6]. Ciguatera fish poisoning is generally thought to be caused by a polyether toxin, usually ciguatoxin (CTX). It is likely however, that the symptom complex we describe as ciguatera, may actually be a result of the consumption of other polyether toxins, such as palytoxin, scaritoxin, maitotoxin and other as of yet unidentified toxins[7].

Ciguatera is not a new disease. The term was coined during the 18th century, when it was noted that a symptom complex would sometimes develop following the ingestion of a marine snail, *Turbo pica,* also commonly known as "cigua"[15]. There were reports of illness due to the consumption of fish noted by the Egyptians during ancient times[12]. There is also evidence to suggest that there were cases of ciguatera poisoning during the voyages of Captain Bligh and Captain James Cook[16,17].

The illness has been extending to new areas however, partly due to modern transportation, that allows fresh fish to be sold in inland areas, and also because of ecological changes that may be contributing to ciguatera endemicity in certain areas of the Pacific. The mechanism of these ecological changes is not well elucidated at this point, but it has been frequently noted that ciguatoxic fish will often increase, or suddenly appear in previously unaffected areas, following an upset in the benthic environment, as may occur during coastal construction projects or dredging, or underwater nuclear bomb testing[13,18].

The primary endemic areas, however, are still the tropical and subtropical coastal regions of the world, particularly in the South Pacific islands and the Caribbean[19,20]. In the United States, most cases occur in Hawaii and in Southeastern Florida, although cases have been reported from Texas, California and occasionally the inland states as the result of importing fish from endemic areas[1-6,12,13,21].

Pathogenesis

It has been determined that ciguatoxin is produced by a photosynthetic benthic dinoflagellate *Gambierdiscus toxicus,* which lives in the coral reef environment[8]. Herbivorous fish consume the organism in algae that contain the toxin and concentrate the CTX in their internal organs and flesh. These fish may then be consumed by larger carnivorous fish, which in turn concentrate the toxin to a greater extent. Thus, the toxin passes up the food chain to the human consumer. The presence of toxic fish tends to be sporadic and unpredictable, making it impossible without the use of scientific testing to determine whether or not a fish caught from a specific area, at a specific time, may be safe to eat.

Individual susceptibility to the toxin varies considerably. A given amount of fish, when consumed by one person may cause illness, whereas another person may remain well. It has been demonstrated that susceptibility to the toxin may increase after a previous exposure, and people who have suffered from ciguatera in the past may actually become more susceptible to the disease[9,10]. Even in the absence of symptoms

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at first exposure, those with frequent intake of ciguatoxic fish are more likely to become ill. This may be a matter of accumulation of CTX in the host, or possibly an immunologic reaction.

It is interesting to note that individuals suffering from ciguatera will often have symptoms after eating *any* seafood, and often nuts, nut oils and alcoholic beverages as well. The mechanism behind this phenomenon is as yet unknown, but it is recommended that individuals suffering from ciguatera follow a diet avoiding such products[11].

The toxin involved in ciguatera is odorless and tasteless. There is no ordinary means of detecting the presence of the toxin other than by scientific testing. The toxin is heat-stable, and is not destroyed by boiling, steaming, baking, smoking, salting, pickling or freezing[12,13,14].

The mechanism whereby the polyether toxins affect a human has not yet been elucidated. Originally it was thought to exert its effect by an anticholinesterase activity, but later it was found to have a more complex mechanism of action which has yet to be determined[22].

Clinical manifestations

The toxin primarily affects the gastrointestinal tract and the nervous system. Within about 4 to 10 hours after ingestion of a toxic fish, the individual typically develops gastrointestinal symptoms: Nausea, vomiting, diarrhea and abdominal cramps, often associated with a feeling of profound weakness and dysphoria. Muscle aches, joint pains, diaphoresis and chills may be present at this time as well. The gastrointestinal symptoms resolve after the first 12 hours of the illness[10,12,13,15,20,21].

Typically it is the neurologic symptoms that cause the prolonged discomfort in the disease. These neurologic symptoms generally begin at about the time the gastrointestinal complaints are resolving, and consist of dysesthesias and paresthesias particularly involving the perioral region and the distal extremities. Classically, one may experience the "temperature reversal phenomenon" whereas cold objects give a warm sensation and touching warm objects results in a cold sensation. Often on drinking cold beverages, the person will describe a feeling of tingling of the tongue; cold beverages may feel hot, and vice-versa. The feeling of paresthesias is usually quite distressing; it may be described by some as a painful burning sensation. Pruritus typically develops as well, about one day after the onset of the initial gastrointestinal complaints. Symptoms usually last about one week, although may persist for months and be exacerbated by the consumption of other food products, as described above.

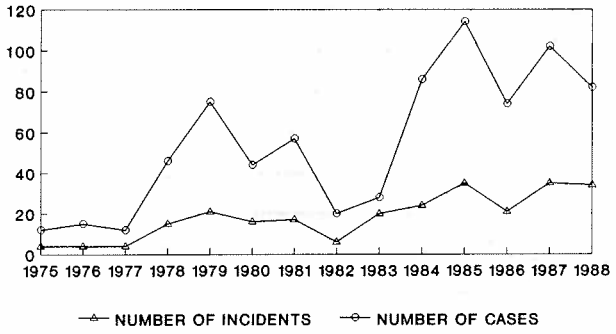
Ciguatera is generally a self-limiting disease, but death may occur as a result of cardiac dysrhythmias, hypotension, shock or cerebral edema. The case-fatality rate varies from 0.1% to 1%, depending on the geographic location[7,11,12,13].

Treatment

There is no specific treatment nor antidote for ciguatera. Treatment is generally symptomatic and consists of the administration of analgesics and specific drugs to treat the complications described above, should they develop.

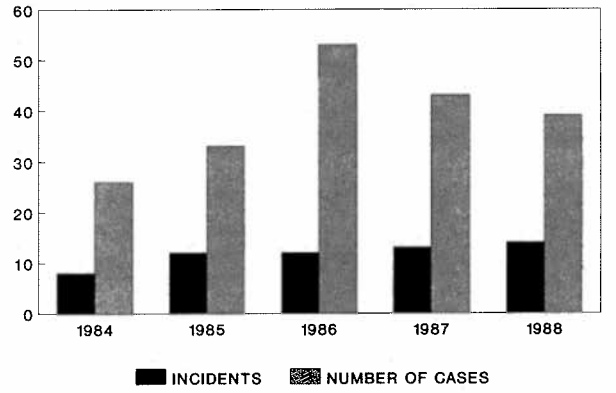
Mannitol, a commonly used diuretic, has been shown to

FIGURE 1:
ANNUAL INCIDENCE OF CIGUATERA
STATE OF HAWAII, 1975 - 1988



SOURCE: HAWAII STATE DEPARTMENT OF HEALTH

FIGURE 2:
CIGUATERA INCIDENTS
ISLAND OF HAWAII, 1984 - 1988



SOURCE: HAWAII STATE DEPARTMENT OF HEALTH

TABLE 1:
ANNUAL INCIDENCE OF CIGUATERA
PER 100,000 POPULATION
BY ISLAND AND YEAR: 1984 - 1988

YEAR	POPULATION	NO. CASES	ANNUAL INCIDENCE PER 100,000 POPULATION
OAHU			
1984	802,351	38	4.7
1985	812,784	29	3.6
1986	818,487	13	1.6
1987	830,597	40	4.8
1988	838,194 est.	27	3.2
KAUAI			
1984	44,167	17	38.5
1985	44,679	47	105.0
1986	46,440	8	17.2
1987	47,600	12	25.2
1988	47,700 est.	6	12.5
MAUI			
1984	74,750	5	6.7
1985	76,462	5	6.5
1986	78,790	0	0
1987	81,100	11	13.6
1988	90,300 est.	10	11.1
HAWAII			
1984	107,169	26	25.2
1985	108,910	33	30.3
1986	112,039	53	47.3
1987	114,434	43	37.6
1988	115,200 est.	39	33.9
STATE			
1984	1,037,206	86	8.3
1985	1,051,481	114	10.8
1986	1,064,732	74	7.0
1987	1,082,500	106	9.8
1988	1,091,394 est.	83	7.5
		TOTAL 462	AVERAGE 8.7

reduce remarkably the intensity and duration of symptoms of ciguatera in a number of patients[23]. As of yet, formal clinical trials using the drug have not been done; the mechanism of action of mannitol is unknown. It may be consequent to diuresis with subsequent rehydration that flushes out the ciguatoxin. It may be a matter of the effects of mannitol on the sodium and potassium channels in the cell membrane. Less likely is the possibility of some type of direct chemical detoxification by the action of mannitol.

It is also recommended that the patient suffering from ciguatera be placed on a "ciguatera diet" which involves avoidance of *all* seafood (even including those which are not usually contaminated with ciguatoxin, such as shellfish), as well as nuts, nut oils, sesame oil and alcoholic beverages until symptoms have completely subsided, in order to prevent the worsening or prolonging of symptoms[11].

Epidemiology

Epidemiological studies have been carried out in the South Pacific and Caribbean ocean areas in order to determine the incidence in these endemic areas. Annual incidence rates varied during the interval 1979 to 1983 from one case per 100,000 people in the Solomon Islands to 1,338 per 100,000 people in Tokelau[19]. Other high incidence areas with rates calculated for the same interval were: French Polynesia with 585 cases per 100,000; Kiribati, with 462 cases per 100,000; and Tuvalu, 484 cases per 100,000[19]. During the years 1982 to 1987 the Marshall Islands had 234.9 cases per 1000 population[18]. A study from St. Thomas, U.S. Virgin Islands, revealed an incidence rate of 36.5 cases per 1,000 population in 5 years[9].

In the Virgin Islands, the most commonly implicated species of fish was the *Caranx ruber* (Carrang). In the South Pacific, in addition to the *Carangidae* (Jacks), *Lycodontis javanicus* (Moray eel) and *Lutjanidae* (snappers) were also highly suspect as the source of ciguatera[25]. In Fiji, the most commonly implicated species was *Sphyraena barracuda* (Barracuda)[24].

A previous epidemiologic investigation of ciguatera in the

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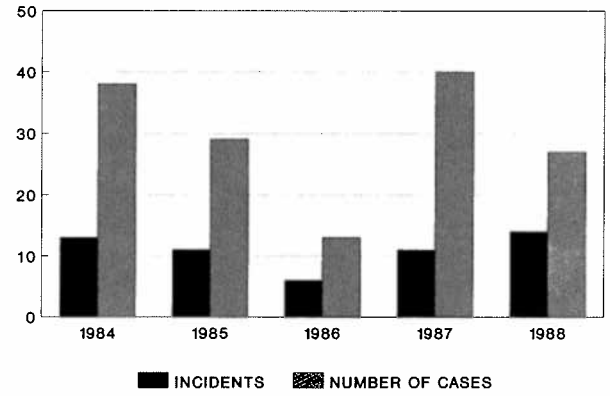
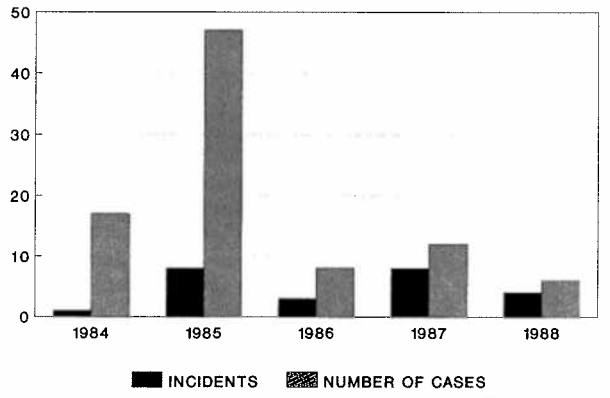
FIGURE 3:
CIGUATERA INCIDENTS
ISLAND OF OAHU, 1984 - 1988



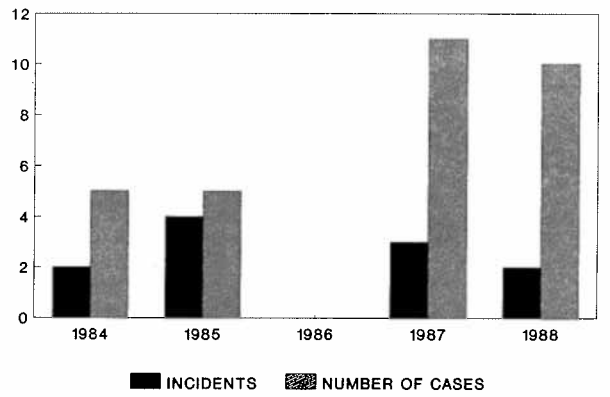
SOURCE: HAWAII STATE DEPARTMENT OF HEALTH

FIGURE 4:
CIGUATERA INCIDENTS
ISLAND OF KAUAI, 1984 - 1988



SOURCE: HAWAII STATE DEPARTMENT OF HEALTH

FIGURE 4:
CIGUATERA INCIDENTS
ISLAND OF MAUI, 1984 - 1988



SOURCE: HAWAII STATE DEPARTMENT OF HEALTH

Hawaiian Islands from 1975 to 1981 revealed an average incidence rate of 1.3/100,000 population. Again, the *Carangoides* species (Jacks or Ulua and Papio) was the most frequently implicated, followed by *Seriola dumerilii* (Amberjack or Kahala), and *Cheilinus rhodochrous* (Wrasse or Po'ou). Other implicated fish included the *Mulloidichtys samoensis* (Goatfish or Weke), *Scaridae* species (Parrotfish or Uhu), *Mugil cephalus* (Mullet or Amaama), *Epinephelus guernus* (Grouper or Hapuupuu) and *Acanthurus dussumieri* (Surgeonfish or Palani)[13].

The Hawaii State Department of Health (DoH) investigates each suspected case of ciguatera that is reported. Every ciguatera investigation involves an environmental, epidemiological and laboratory examination. The epidemiological investigation consists of determining the basic demographics of the cases: The timing and location of the outbreak; determining the parts of the fish eaten; the extent of symptoms; whether hospitalized; the number of work days missed and the duration of illness. This information is usually obtained by interviewing the patients and often their physicians as well.

The laboratory investigation includes the collection of any leftover fish samples and testing them with an ELISA test to determine semi-quantitatively the amount of polyether toxin present in the fish. This is done by a stick-test developed at the University of Hawaii[26].

The environmental investigation involves determining the place where the fish was caught or purchased; often means making a site-visit to the market or restaurant where the fish was obtained. Companion samples of fish from the same catch may also have to be tested. The merchant is advised not to sell any fish of the same species from the same catch, nor remaining parts of the same fish. The place of catch and the species of the fish is recorded (if available) and the involved merchants are given information about ciguatera and other types of fish poisoning.

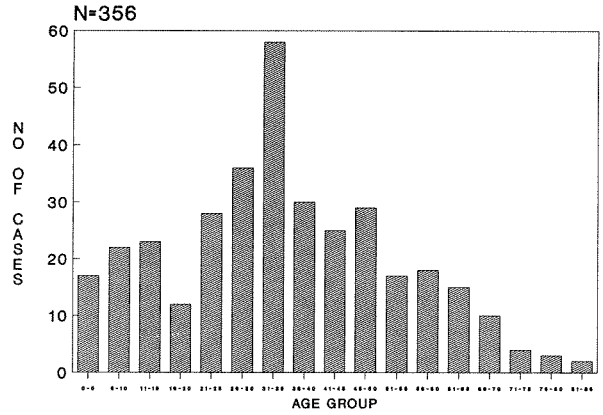
Materials and methods

DoH records of all reported ciguatera incidents were reviewed for the 5-year period 1984 to 1988. All probable or confirmed incidents were included in the investigation. Cases that occurred as the result of eating fish that were caught outside of the State were included.

A "probable" case was defined as "experiencing both gastrointestinal and paraesthetic symptoms within 30 hours following the consumption of a fish implicated in ciguatera". A confirmed case was defined as "a person with signs and symptoms compatible with ciguatera plus a positive poke-stick test of leftover fish eaten by that person." The term "incident" was used as opposed to "outbreak"; an outbreak generally refers to more than one person being ill, whereas an incident may refer to a single case. A person epidemiologically linked to an incident with a confirmed case and exhibiting at least some components of the gastrointestinal or neurological symptoms also was considered as a confirmed case. Information extracted from each chart included: The date of onset and location of the incident; the age and sex of the victims; the species of fish eaten; the place where the fish was obtained; and the parts of the fish consumed.

The species of fish involved was usually identified by a common or Hawaiian name by those who saw the fish before

FIGURE 6:
CIGUATERA INCIDENTS
ISLAND OF HAWAII, 1984 - 1988



SOURCE: HAWAII STATE DEPARTMENT OF HEALTH

it was consumed. Occasionally fish markets had to be consulted regarding the correct nomenclature, and in only one instance was the type of fish unknown.

Several incidents occurred after the consumption of more than one type of fish. In these cases, the names of all the fish that may have been involved were recorded. The stick-test results of the fish were recorded as positive, borderline or negative, and were designated as either from the fish eaten or a companion sample (fish of the same species, caught at the same time and same location as the original fish).

In order to help determine if there were unreported cases, emergency room records in 6 different hospitals throughout the State were reviewed in order to find cases with the diagnosis of ciguatera. None was found. The hospitals chosen were those whose record-keeping systems allowed such investigations to be performed. The information was stored and analyzed using the D-Base III plus program on a Wang PC-compatible computer at the DoH office. Graphs were produced by *Harvard Graphics.*

Results

A total of 150 incidents were reported during the years 1984 to 1988 in the State of Hawaii. These incidents occurred in all 4 counties of the State and were investigated by the DoH Epidemiology branch. The150 incidents (57 confirmed, 93 probable) involved 462 cases of ciguatera. There were 652 exposed individuals; the 462 cases, therefore, comprised an overall attack rate of 70.9%. However the attack rate varied greatly in each outbreak; some outbreaks had attack rates of 100%. The island of Hawaii reported the most incidents, followed by Oahu, Kauai and Maui respectively (Table 1).

Although a significant increase in cases and incidents had been noted during the late 1970s and early 1980s, such increases have not been noted for the 1984 to 1988 period (see Figure 1). The island of Hawaii reported 8, 12, 12, 13, and 14 ciguatera incidents during each of the years from 1984 through 1988 (Figure 2). The other islands did not show significant increases during the same 5-year period (Figures 3, 4 and 5).

Kauai had 105 cases/100,000 population in 1985 primarily due to a problem with toxic *Ctenochaetus strigosus* (kole) fish

TABLE 2:
INCIDENTS OF CIGUATERA BY SPECIES OF FISH IMPLICATED, STATE OF HAWAII: 1984 - 1988

NAME OF FISH	NUMBER OF INCIDENTS
Ulua	19
Papio	16
Kole	15
Wahanui	12
Roi	7
Po'ou	6
Weke	4
Barracuda	4
Eel	3
Kahala	3
Palani	3
Uku	3
Ta'ape	3
Mullet	3
Opakapaka	2
Omilu	2
Moana	2

Fish may be implicated more than once.

TABLE 3:
INCIDENCE OF CIGUATERA BY AREA CAUGHT AND ISLAND: 1984 - 1988

AREA CAUGHT	NO. OF INCIDENTS
OAHU	
Reef Runway	3
Kaena Point	3
Barbers Point	2
Haleiwa	2
Waianae Coast	2
Waianae	2
HAWAII	
South Kona	7
Milolii	7
South Point	6
Kawaihae	4
Keei	4
Puako	4
Kona	2
Punaluu	2
MOLOKAI	2
KAUAI	
Napali Coast	7
Nualolo	2

Fish may be implicated more than once.

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FIGURE 7:
CIGUATERA INCIDENTS 1984 - 1988

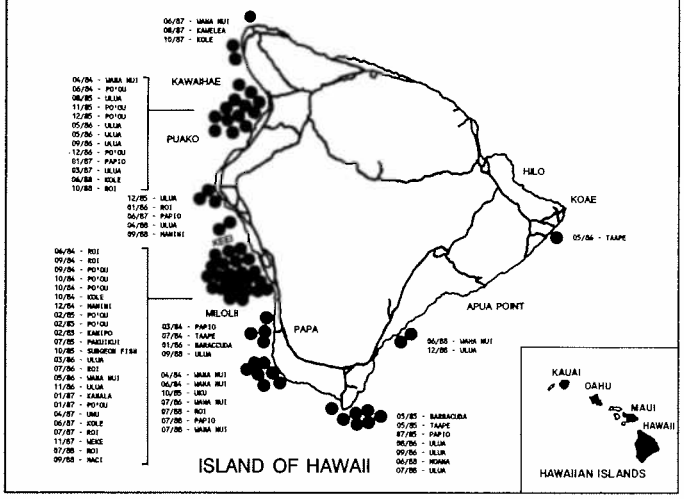
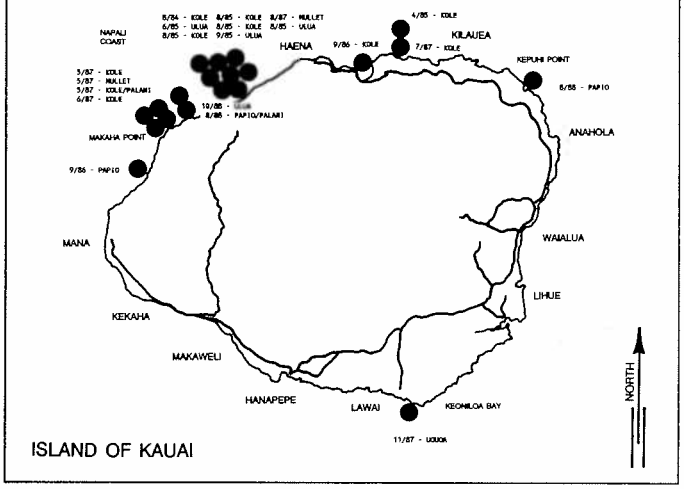


FIGURE 8:
CIGUATERA INCIDENTS 1984 - 1988



on the Napali coast.

The sex differential was 182 male patients and 174 females. An age distribution curve shows a peak in the early fourth decade of life (Figure 6).

The most frequently impugned species of fish were the Papio and Ulua causing a total of 35 incidents (Table 2). Kole were implicated in 15 ciguatera incidents. The third most frequently involved fish was the Wahanui (*Aphareus furcatus* or fork-tailed snapper) in 12 incidents. Other fish involved in more than one ciguatera incident included: Roi (*Cephalophilus guttatus* blue-spotted grouper); Po'ou; Weke; Barracuda); eel; Kahala; Palani; Uku (*Aprion virescens* gray snapper); Ta'ape (*Lutjanus kasmira* blue-lined snapper); Mullet; Opakapaka (*Pristipomoides filamentosus* snapper); Moana (*Parupeneus multifasciatus* goatfish); and Omilu (*Caranx melampygus* blue crevally). There were additional individual incidents involving consumption of more than one of the above fish at a time, or other fish whose common names were: Sea bass, shark, rainbow runner, blue-lined surgeonfish,

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FIGURE 9:
CIGUATERA INCIDENTS 1984 - 1988

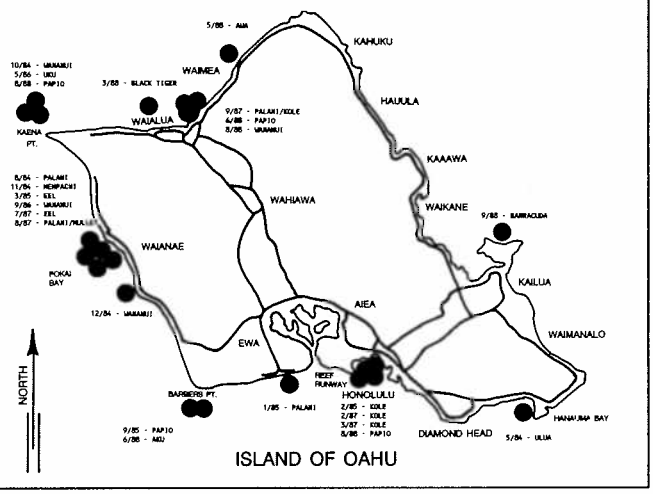


FIGURE 10:
CIGUATERA INCIDENTS 1984 - 1988

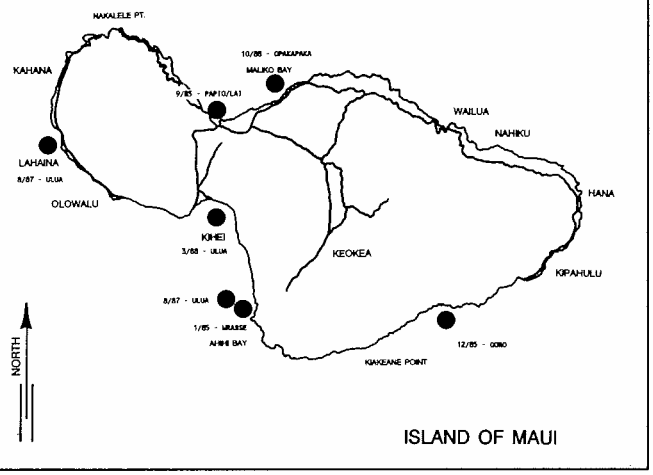
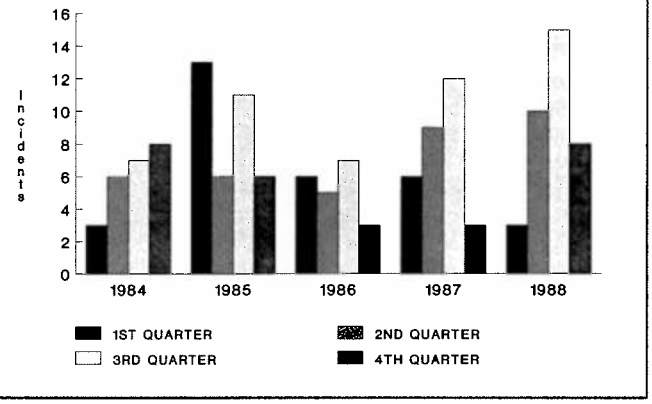


FIGURE 11:
INCIDENTS OF CIGUATERA BY QUARTER:
1984 - 1988



smoked mackerel from the Philippines (*Tinapa Galongong*), Wahoo, false mullet, Japanese barracuda, Achilles tang, black trigger, milkfish, convict tang, squirrel-fish, porgy and red snapper. Oddly, there was one outbreak attributable to the consumption of octopus and another to Aku.

The Kona coast of the island of Hawaii was responsible for the most incidents (Table 3). These fish were primarily caught by sportfishing off the Napali Coast of Kauai, South Point of Hawaii, Kaena Point, Barber's Point, Pokai Bay and the Waianae coast of Oahu (Figures 7, 8, 9 and 10). In addition to the sites represented on the maps, there were 2 episodes of ciguatera attributable to fish caught off Molokai, and one off the island of Lanai.

No marked seasonal variation was observed in ciguatera incidents, although there was a slight increase noted during the third quarter of the year (July through September), and a decrease during the fourth quarter (October through December) during the 5-year period studied (Figure 11).

Of the 150 known ciguatera incidents, in 130, records were kept indicating the parts of the fish that were consumed. In 59, parts of the fish other than the flesh, such as the head, viscera and roe, or a soup made from these parts, were consumed by at least one of the individuals who became ill .

Commercially sold fish accounted for 33 out of the 150 ciguatera incidents (22%). These fish were either consumed in a restaurant or were purchased from markets. The other 78% of incidents were attributable to fish caught recreationally.

In 89 incidents fish were available for testing using the stick-test, either leftovers of the fish actually eaten or fish from a companion catch. The putative fish itself was available for testing in only 61 incidents.

Discussion

The statewide incidence rate of 8.7/100,000 shows a significant increase over the previous epidemiologic study of 1975 to 1981 that demonstrated an incidence of 3/100,000[13]. The increase occurred largely during the early 1980s (Figures 1 and 2). (In referring to the figures, it is important for the reader to realize that the number of incidents correlates more closely with the actual endemicity of ciguatera at a given period of time rather than with the number of cases; the latter relates to the number of people who ate the toxic fish. Thus, a single outbreak affecting 100 people would be of less consequence epidemiologically than 100 different fish making 100 people ill.) This may be a result of increased awareness of the disease and better reporting, but it is also likely that there actually has been an increase in ciguatera in the Hawaiian Islands. This may be due to changes in the reef environment similar to what has occurred in the Marshall islands[18].

In the last 5 years, however, the ciguatera rates seem to have reached a plateau. The areas typically affected are the leeward coastal areas. Areas of dredging and construction will often show an increase in ciguatoxic fish, such as when the reef-runway at Honolulu International Airport was constructed. Construction lasted from May 1973 to December 1977. The first toxic fish began to be recorded in April, 1978, 4 months after the construction ceased, and toxic fish are still known to inhabit the region. The Pokai Bay area of the Waianae Coast underwent construction of a breakwater from April 1977 to

January 1979; it involved dredging, filling and blasting. After 15 months, reports of toxic fish began appearing, and to the present, the Pokai Bay area is known for its ciguatera problem[13]. The large increase in reported cases from the Kona coast of the Big Island may also be related to the multiple construction projects that occurred earlier this decade.

The age of onset of the disease correlates well with the ages of individuals more likely to be out fishing. If it is true that the susceptibility to ciguatoxin increases with repeated previous exposure, one would expect that older age groups with more years of exposure to ciguatoxin would have more cases of illness. Age distributions in other studies have been similar[9,27].

The slight increase in the number of ciguatera incidents during the third quarter of the year may be due to climatic changes of the reef environment, or an increase in fishing activity during that time of the year. The decrease during the fourth quarter may be due to cooler and increasingly rainy weather. A seasonal study from Puerto Rico showed definite seasonal trends with peak seasons for ciguatoxic barracuda occurring in January to May, and August to November[28].

In 59 of the 150 ciguatera incidents, at least one (and usually more) of the victims consumed a portion of the fish known to concentrate the ciguatoxin, notably the gut, liver, head and roe, as well as a soup or broth made of the latter. It is likely that many, if not most, of these outbreaks (a large proportion of the total) could have been avoided if the individuals involved had been educated regarding ciguatera and the concentration of the ciguatoxin in these parts of the fish.

Ciguatera is of great concern at local fish markets, which attempt to avoid the sale of toxic fish by avoiding buying fish caught near leeward reefs, as well as avoiding the sale of specific species known to be toxic. The Kahala is an example of a fish that is no longer sold in local markets due to its high prevalence for ciguatoxicity.

The use of the stick-test for commercial use does not appear to be cost-effective. It is reassuring to know that in the year 1987, among a total of 164,910 reef fish caught commercially, only 5 incidents of ciguatera poisoning were reported, only .003% of the total reef fish caught. The year 1987 is representative of other years as well, in which commercial ciguatoxic fish have only been implicated, ie in 3 to 10 incidents per year during the years 1984 to 1988.

The major source of ciguatera cases has been the fish caught by sportfishing, typically on weekends and holidays. If people could be educated to avoid consuming heads, viscera and roe of reef fish (especially a soup made of the above); and avoid fish caught in the areas known for being ciguatera-prone, the rates of ciguatera would decrease dramatically. The addition of the stick-test for use in sportfishing could reduce the rates of illness even more .

Since the future incidence of ciguatera is unpredictable, we cannot assume the problem will go away. We can, however, significantly reduce the probability of future outbreaks by educating the public, and by encouraging the use of the stick-test in sportfishing.

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REFERENCES

1. Ragelis EP: Ciguatera Seafood Poisoning: Overview. In: *Seafood Toxins*, p.4 (Ragelis, EP, Ed.). Am Chem Soc Symp Series, no. 262.
2. Ciguatera Fish Poisoning, Maryland, Centers for Disease Control. *MMWR*, 1980;29:610.
3. Todd E, Szabo R. Ciguatera Poisoning-First Confirmed Report in Canada. *Canadian Diseases Weekly Report*, 1983;8:174-176.
4. Ho AM, Fraser IM, Todd EC: Ciguatera Poisoning. A Report of Three Cases. *Ann Emerg Med*, 1986;15:1225-8.
5. Cohen L, MacLean JD, Lalonde R: Ciguatera Fish Toxin Poisoning: An Outbreak in Canadian Tourists in the Dominican Republic. *Canadian Diseases Weekly Report*, 1987;12:73-75.
6. Frenette C, MacLean JD, Cedilotte L: Ciguatera — A Large Common Source Outbreak in Canadian Vacationers in Cuba. *Canadian Diseases Weekly Report*, 1987;13:87-8.
7. Withers NW: Ciguatera Fish Poisoning. *Ann Rev Med*, 1982;33:97-111.
8. Campbell B, Nakagawa LK, Kobayashi MN, Hokama Y: *Gambierdiscus Toxicus* in Gut Content of the Surgeonfish *Ctenochaetus Strigosus* (Herbivore) and its Relationship to Toxicity. *Toxicon*, 1987;10:1125-1127.
9. Morris JG, Lewin P, Smith CW, Blake PA, Schneider R: Ciguatera Fish Poisoning: Epidemiology of the Disease on St Thomas, U.S.Virgin Islands. *Am J Trop Med Hyg*, 1982;31(3):574-578.
10. Helfrich P: Fish Poisoning in Hawaii. *Hawaii Med J*, 1963;22:361-372.
11. Bach F, Terrell-Perica S: Ciguatera Fish Poisoning in the Pacific, in *South Pacific Commission Information Circular*. Serial No: 115, July-September 1988.
12. Lange WR: Ciguatera Toxicity. *AFP* 1987;35:177-182.
13. Anderson BS, Sims JK, Wiebenga NH, Sugi MS: The Epidemiology of Ciguatera Fish Poisoning in Hawaii 1975-1981. *Hawaii Med J*, 1983;42:326-334.
14. Dembert ML, Strosahl KF, Bumgarner RL: Diseases from Fish and Shellfish Ingestion. *AFP*, 1981;24:103-108.
15. Hokama Y: Ciguatera Fish Poisoning. *Journal of Clinical Laboratory Analysis*, 1988;2:44-50.
16. Steinfeld AD, Steinfeld HJ: Ciguatera and the Voyage of Captain Bligh. *JAMA*, 1974;228:1270-1271..
17. Cooper MJ: Ciguatera and Other Marine Poisoning in the Gilbert Islands. Pacific Science Vol. XVIII, No. 4, pp. 411-440, 1964.
18. Ruff TA: Ciguatera in the Pacific: A Link With Military Activities. *Lancet*, 1989;1(8631):201-205.
19. Lewis, ND: Disease and Development: Ciguatera Fish Poisoning. *Soc Sci Med, 1986;*23:983-993..
20. Morris JG, Lewin P, Hargrett NT, Smith CW, Blake PA, Schneider R: Clinical Features of Ciguatera Fish Poisoning. A Study of the Disease in the US Virgin Islands. *Arch Intern Med*, 1982;142:1090-1092.
21. Lawrence DN, Enriquez MB, Lumish RM, Maceo A: Ciguatera Fish Poisoning in Miami. *JAMA*, 1980;244:254-258.
22. Rayner MD, Kosaki TI, Fellmeth EL: Ciguatoxin: More than an Anticholinesterase. *Science*, 1968;160:70-71.
23. Palafox NA, Jain LG, Pinano AZ, Gulick TM, Williams RK, Schatz IJ: Successful Treatment of Ciguatera Fish Poisoning with Intravenous Mannitol. *JAMA*, 1988;259:2740-2742.
24. Sorokin M: Ciguatera Poisoning in North-West Viti Levu, Fiji Islands. *Hawaii Med J*, 34,207-210. 1975.
25. Bagnis, R: Clinical Aspects of Ciguatera (Fish Poisoning) in French Polynesia. *Hawaii Med J*, 1968;28:25-28.
26. Hokama Y: A Rapid, Simplified Enzyme Immunoassay Stick Test For the Detection of Ciguatoxin and Related Polyethers from Fish Tissues. *Toxicon*, 1985;23:939-946.
27. Bagnis R, Kuberski T, Laugier S: Clinical Observations on 3,009 Cases of Ciguatera (Fish Poisoning) in the South Pacific. *Am J Trop Med Hyg*, 1979;23(6):1067-1073.
28. Tosteson TR, Ballantine DL, Durst HD: Seasonal Frequency of Ciguatoxic Barracuda in Southwest Puerto Rico. *Toxicon*, 1988;26:795-801.

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